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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Ivor R. Elrifi
Mintz, Levin, Cohn, Ferris,
Glovsky and Popeo, P.C.
One Financial Center
Boston, MA 02111

EXAMINER	
CHUNDURU, SURYAPRABHA	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 10/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/766,863	POWELL ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,7,10-15 and 17-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,7,10-15 and 17-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action filed on July 27, 2004 have been entered.

2. Claims 1-3, 6-7, 10-15, 17-20 are pending. Claims 4-5, 8-9, 16 are cancelled.

Response to arguments

3. Applicants' response to the office action is fully considered and found to be persuasive in part.

4. The following is the rejections made in the previous office action under 35 USC 102(b):

A. Claims 1, 2, 6-7, 10-13,15 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Harris et al. (USPN. 5,985,829).

Harris et al. teach a method of claim 1, 6, and 19, of identifying the function of a test compound (a polypeptide) comprising

(i) providing multiple cell types (see column 10, lines 58-67), wherein the cell types comprise fibroblast (normal and mutant cell types), hematopoietic cells or cells from hematopoietic system, lymphoblastic system (which include T-cell, B-cell), and cells from lung and nervous system (see column 2, lines 37-43);

(ii) contacting each cell types with a test compound (see column 22-31, column 10, lines 16-20);

(iii) measuring expression of one or more genes in each cell type (expression of p53, and /or helicase activity, see column 10, lines 20-23, column 2, 43-67);

wherein an alteration in the expression of one or more genes in each cell type in the absence of the test compound indicates the function of said test compound (see column 2, lines 28-30column 10, lines 20-23, column 9, lines 6-7).

With regard to claim 2, and 7, Harris et al. teach that expression of at least two genes or three or more genes is measured in each cell type (see column 2, lines 28-30, column 10, lines 20-23, column 9, lines 6-7, for p53 and helicase gene activity column 6, lines 5-20, for RNA polymerase II or ATPase activity);

With regard to claim 10, Harris et al. teach cell types are provided in a container (culture plates, seeded on cover slips, see column 19, lines 64-67);

With regard to claim 11, expression of one or more genes is compared to expression of a reference gene (control, column 9, lines 5-7, column 2, lines 11-31);

With regard to claim 12, test compound modulates expression of said one or more genes at least 4-fold relative to reference gene (wild-type p53, see column 20, table 1, lines 25-44);

With regard to claim 13, said test compound is a polypeptide (see column 11, lines 18-43);

With regard to claim 15, cell types comprise human cells (see column 19, lines 64-67). Thus the disclosure of Harris et al. meets the limitations in the instant claims.

Response to arguments:

Applicants' arguments with regard to the above rejection and found not persuasive. Applicants argue that Harris et al. teach a method for screening compounds for their ability to induce apoptosis and did not teach screening compounds for their ability to modulate any function and there fore the instant invention is not within the scope described by Harris et al. These arguments are fully considered and found not persuasive. As pointed out by the applicants, the instant invention encompasses any function that is modulated by a compound, which

indicates that any function includes function related to apoptosis. It is related as genus species combination. Thus the disclosure of Harris et al. does anticipate the instant claims.

Applicants' further argue that Harris et al. did not teach measuring gene expression, rather teaches measuring enzyme activities and points out to Fig.6 of the patent. These arguments are fully considered and found not persuasive. Examiner notes that the activities are measured indirectly based on the p53 mRNA expression levels. Thus the disclosure of Harris et al. does teach measuring mRNA expression levels as an indication of the activities of these said enzymes. Thus the disclosure of Harris et al. does anticipates the instant claims and therefore the rejection is maintained herein.

5. With regard to the rejection made in the previous office action under 35 USC 102(e) as anticipated by Garner (USPN. 6,657,758), Applicants arguments regarding a compound, which does not include UV radiation, are found to be persuasive and the rejection is withdrawn herein in view of the arguments.

6. With regard to the rejection made in the previous office action under 35 USC 103(a) as being unpatentable over Johnson et al. in view of Kamb et al., Applicants arguments and amendment are fully considered and the rejection is withdrawn in view of the amendment.

7. The following are the rejections made in the previous office action under 35 USC 103(a) :

A. Claims 3 and 14 rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. (USPN. 5,985,829) and in view of Friend et al. (USPN. 6,303,291).

Harris et al. teach a method of identifying the function of a test compound (a polypeptide) comprising (i) providing multiple cell types (see column 10, lines 58-67), wherein the cell types comprise fibroblast (normal and mutant cell types), hematopoietic cells or cells from

hematopoietic system, lymphoblastic system (which include T-cell, B-cell), and cells from lung and nervous system (see column 2, lines 37-43); (ii) contacting each cell types with a test compound (see column 22-31, column 10, lines 16-20); (iii) measuring expression of one or more genes in each cell type (expression of p53, and /or helicase activity, see column 10, lines 20-23, column 2, 43-67); wherein an alteration in the expression of one or more genes in each cell type in the absence of the test compound indicates the function of said test compound (see column 2, lines 28-30column 10, lines 20-23, column 9, lines 6-7).

Harris et al. also teach that (a) expression of at least two genes is measured in each cell type (see column 2, lines 28-30, column 10, lines 20-23, column 9, lines 6-7, column 6, lines 5-20); (b) cell types are provided in a container (culture plates, seeded on cover slips see column 19, lines 64-67); (c) expression of one or more genes is compared to expression of a reference gene (control, column 9, lines 5-7, column 2, lines 11-31); (d) test compound modulates expression of said one or more genes at least 4-fold relative to reference gene (wild-type p53, see column 20, table 1, lines 25-44); (e) said test compound is a polypeptide (see column 11, lines 18-43); (f) cell types comprise human cells (see column 19, lines 64-67).

However, Harris et al. did not teach expression of at least five genes in each cell type, contacting cell types with two or more test compounds.

Friend et al. teach a method for identifying the functions of a drug in a cell type, wherein Friend et al. teach that the method comprises (i) detection of gene expression of 50 genes at a given time (which includes the limitation of claim 3, i.e., expression of at least five genes, see column 14, lines 50-56); (ii) contacting the cell types with two or more test compounds (column 4, lines 58-60).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of drug target screening as taught by Harris et al. with the method of Friend et al. which is applicable to screen a large number of drug targets using an array system because Friend et al. taught that a faster and less expensive high through put array system to identify multiple primary targets in cell through which a drug acts on the cell, based on the interpretation of gene expression data(see column 3, lines 1-34). An ordinary practitioner would have been motivated to combine the method of Harris et al. with the high throughput assay system as taught by Friend et al. in order to achieve the expected advantage of developing a high throughput array method for screening a test compound because incorporation of the limitations taught by Friend et al. would reduce cost and time and allows the development of a high-throughput analysis method.

Response to arguments:

With regard to the above rejection Applicants arguments are fully considered and found not persuasive. Applicants argue that Harris does not teach measuring gene expression and Friend does not cure the deficiency . Further Applicants argue that Friend teaches contacting the cells with each compound individually and does not teach contacting the cell types with two or more compounds simultaneously. These arguments are fully considered and found not persuasive because first, as discussed above Harris does teach measuring gene expression and second, Examiner notes that the instant claim 14 does not recite contacting the compounds 'simultaneously' and thus the limitation (simultaneously) is not found in the instant claim 14. Thus the broader scope of the claims do not exclude contacting compounds individually, which

comprises contacting the same cell line with different compounds. Thus the rejection is proper and is maintained herein.

B. Claims 18, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. (USPN. 5,985,829) and in view of Aller (USPN. 6,479,241).

Harris et al. teach a method of identifying the function of a test compound (a polypeptide) comprising (i) providing multiple cell types (see column 10, lines 58-67), wherein the cell types comprise fibroblast (normal and mutant cell types), hematopoietic cells or cells from hematopoietic system, lymphoblastic system (which include T-cell, B-cell), and cells from lung and nervous system (see column 2, lines 37-43); (ii) contacting each cell types with a test compound (see column 22-31, column 10, lines 16-20); (iii) measuring expression of one or more genes in each cell type (expression of p53, and /or helicase activity, see column 10, lines 20-23, column 2, 43-67); wherein an alteration in the expression of one or more genes in each cell type in the absence of the test compound indicates the function of said test compound (see column 2, lines 28-30, column 10, lines 20-23, column 9, lines 6-7).

Harris et al. also teach that (a) expression of at least two genes is measured in each cell type (see column 2, lines 28-30, column 10, lines 20-23, column 9, lines 6-7, column 6, lines 5-20); (b) cell types are provided in a container (culture plates, seeded on cover slips see column 19, lines 64-67); (c) expression of one or more genes is compared to expression of a reference gene (control, column 9, lines 5-7, column 2, lines 11-31); (d) test compound modulates expression of said one or more genes at least 4-fold relative to reference gene (wild-type p53, see column 20, table 1, lines 25-44); (e) said test compound is a polypeptide (see column 11, lines 18-43); (f) cell types comprise human cells (see column 19, lines 64-67).

However, Harris et al. did not teach measuring expression using real-time polymerase chain reaction.

Aller teaches a high throughput screening assay to identify the function of a test compound wherein Aller teach culturing cells in a microplate along with a test compound and measuring expression of one or more genes using real time PCR (see column 1, lines 63-67, column 2, lines 1-55, column 6, lines 30-60). Aller also teaches use of any cell line which can be cultivated in vitro and specifically cell lines are selected from cells expressing cancer genes, apoptosis, DNA damage or loss of heterozygosity (see column 3, lines 2-15, table-1).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of drug target screening as taught by Harris et al. with the method of Aller et al. because Aller taught that the combination of robotics, standard molecular biology techniques (e.g., cell lysis, RNA isolation, reverse transcription), and real time PCR yields a high-throughput analysis and avoids contamination (see column 2, lines 33-41). An ordinary practitioner would have been motivated to combine the method of Harris et al. with the combination of techniques as taught by Aller in order to achieve the expected advantage of developing a high throughput analysis method for screening a test compound because incorporation of the limitations taught by Aller would reduce contamination and allows the development of a high throughput analysis method.

Response to arguments:

With regard to the above rejection Applicants' arguments are fully considered and found not persuasive. Applicants argue that Harris does not teach measuring gene expression and Aller does not cure this deficiency. Applicants' arguments are fully considered and found not

persuasive because as discussed above Harris does teach measuring gene expression and thus it is obvious to modify the teachings of Harris with the teachings of Aller as discussed in the above rejection. Thus the rejection is maintained herein.

8. With regard to the rejection made in the previous office action under 35 USC 103(a) as being unpatentable over Harris et al. (USPN. 5,985,829) and in view of Johnson et al. (WO 99/37817), Applicants arguments and amendment are fully considered and the rejection is withdrawn in view of the amendment.

New Grounds of rejections necessitated by amendment

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. (USPN. 5,985,829) and in view of Gimeno et al. (USPN. 6,008,014).

Harris et al. teach a method of identifying the function of a test compound (a polypeptide) comprising (i) providing multiple cell types (see column 10, lines 58-67), wherein the cell types comprise fibroblast (normal and mutant cell types), hematopoietic cells or cells from hematopoietic system, lymphoblastic system (which include T-cell, B-cell), and cells from lung and nervous system (see column 2, lines 37-43); (ii) contacting each cell types with a test compound (see column 22-31, column 10, lines 16-20); (iii) measuring expression of one or more genes in each cell type (expression of p53, and /or helicase activity, see column 10, lines 20-23, column 2, 43-67); wherein an alteration in the expression of one or more genes in each cell type in the absence of the test compound indicates the function of said test compound (see column 2, lines 28-30column 10, lines 20-23, column 9, lines 6-7).

Harris et al. also teach that (a) expression of at least two genes is measured in each cell type (see column 2, lines 28-30, column 10, lines 20-23, column 9, lines 6-7, column 6, lines 5-20); (b) cell types are provided in a container (culture plates, seeded on cover slips see column 19, lines 64-67); (c) expression of one or more genes is compared to expression of a reference gene (control, column 9, lines 5-7, column 2, lines 11-31); (d) test compound modulates expression of said one or more genes at least 4-fold relative to reference gene (wild-type p53, see column 20, table 1, lines 25-44); (e) said test compound is a polypeptide (see column 11, lines 18-43); (f) cell types comprise human cells (see column 19, lines 64-67).

However, Harris et al. did not teach cell types selected from the group consisting of MG-63 cells, U87-MG cells, TF-1cells, THP-1 cells, HUVEC cells, CCD-1070SK cells and Jurkat E6-1 cells.

Gimeno et al. teach a method for identifying the functions of a drug in a cell based systems, wherein Gimeno et al. teach that the method comprises one or more cell types which include THP-1 cells, HUVEC cells, U937, Hela cells, COS-7 cells (see col. 42, line 20-35).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of drug target screening as taught by Harris et al. with the step of including the cell types as taught by Gimeno et al. which is applicable to screen drug targets for alteration in lipid metabolic pathway genes because Gimeno et al. taught that cell-based assays would provide in identifying agonists/ antagonists that modulate expression of genes involved in lipid metabolic signal pathway cascade (See col. 41, line 65-67, col. 42, line 1-20). An ordinary practitioner would have been motivated to combine the method of Harris et al. with the cells lines as taught by Gimeno et al. in order to achieve the expected advantage of developing a sensitive method for screening a test compound which would allow screening compounds related to alter lipid related genes and aid in identifying therapeutic compounds for treating cardiovascular diseases.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
October 25, 2004

JEHANNE SITTON
PRIMARY EXAMINER
10/26/04